

Fear of avascular necrosis in COVID survivors is real: A rare case series

¹Dr. Arjun A, ²Dr. Gopi HG, ³Dr. Kiran V, ⁴Dr. Chaithra CM, ⁵ Dr. Nagesh Sherikar

^{1,2,3,5}Senior Resident, Department of Orthopaedics, MMCRI, Mysore, Karnataka, India

⁴ Senior Resident, Department of Ophthalmology, MMCRI, Mysore, Karnataka, India

Corresponding Author:

Dr. Chaithra CM

Abstract

COVID-19' can affect different body systems. At present, osteo necrosis of femoral head as a sequelae of 'COVID-19' is rarely documented. By large-scale use of life-saving corticosteroids in COVID-19 cases, we anticipate that there will be a resurgence of AVN cases. We report a series of two cases in which patients developed AVN of the femoral head after being treated for COVID-19 infection. The mean dose of corticosteroid used in these cases was 600 mg (400–1250mg), which is less than the mean cumulative dose of around 2000 mg steroid, documented in the literature as causative for AVN. Patients were symptomatic and developed early AVN of bilateral hip at a mean of 42 days after COVID-19 diagnosis as compared with the literature which shows that it generally takes 6 months to 1 year to develop AVN post steroid exposure. Both the patient had significant dysfunction of coagulation with altered parameters. Thorough ophthalmic examination was done to both. literature has showed micro thrombi in eye, heart, liver, kidney, etc. Is corticosteroid being just a confounding factor??

Keywords: Fear, avascular necrosis, COVID survivors

Introduction

Background

Osteonecrosis of femoral head is most commonly seen in middle age causes are not known one of the cause like Steroid abuse with cumulative dosage of 2g and other cause like viral infections such as HIV, CMV, hepatitis, rubella, rubeola, varicella are also documented to cause osteonecrosis Currently is it due to Covid 19 infection or steroids?

Hypercoagulability state in Covid 19

Cytokine storm pro-inflammatory cytokines like interleukin 6 (IL-6), IL-17A, and tumor necrosis factor α severe infection with COVID-19. Hypercoagulability is a usual finding in inflammation. Pro-inflammatory cytokines have a role in the platelet aggregation and intravascular clot formation and are also involved in the down regulation of physiological anticoagulant pathways in the body but no studies as shown Covid 19 as a primary cause

Case scenario: 1

38 year old male who got infected with Covid 19 who was treated in the ICU for two weeks patient blood parameters were deranged with altered coagulation profile patient treated with steroid with cumulative dose of 1200mg steroids for two weeks, after 65 days patient developed a pain in both the hips which is a sudden in onset which dragging pain with disturbed sleep difficult in doing his regular activities, significantly walking distance has been reduced. X-ray and MRI has taken it showed a Ficat-Arlet stage II.

Since patient under stage 2 A patient posted for bilateral decompression post operatively patient relieved with pain post operatively at 6 months patient doesn't have a pain and doing well.

Case scenario: 2

A 26-year-old male patient was diagnosed with COVID-19 on 15 March 2020, for which patient received an intravenous methylprednisolone (600mg). Sixty days post COVID-19 detection, the patient developed pain in the bilateral groin. The patient had no history of hip pain in the past. Radiographs and MRI were done 50 days post COVID-19 detection that showed bilateral hip AVN (Ficat-Arlet stage II).

Outcome and follow-up the mean dose of prednisolone equivalent steroid taken by the patient in our series was 900mg. The time duration for the development of AVN post COVID-19 diagnosis in our report of average of 62.5 days, all the three patients were started on oral alendronate 70mg weekly dosages along with intravenous zoledronic acid 5mg annually. At last mean follow up of 3 months, second patient with stage 2 doesn't required surgery and were comfortable. Mean Visual Analogue Score for pain reduced from 8 to 2 at the mean follow-up of 90 days. But case scenario 1 with stage 2 A again developed a pain repeat MRI shows progression of disease so decided to do a TOTAL hip arthroplasty.

Discussion

COVID-19, which is produced by SARS-CoV-2, is impacting a large number of people around the world. The virus is responsible for the deaths of a large number of people. Although many patients are healing from COVID-19, it is crucial to remember that sequelae, including non-pulmonary consequences, may occur after recovery. Avascular necrosis (AVN) is one of these problems, which if left untreated can result in severe consequences and bone collapse. SARS has a lot of AVN, and COVID-19 infection may have a lot of it as well. It's important to remember that individuals who have recovered from COVID-19 infection, such as SARS, are still at risk of contracting AVN.

For certain COVID-19 situations, several guidelines recommend corticosteroids. Although corticosteroids are not recommended for routine use, they are indicated in some situations, such as COPD or asthma exacerbation, or septic shock, according to the WHO. ² The Surviving Sepsis Campaign recommends (in the form of a weak recommendation) the use of systemic corticosteroids in patients with Acute Respiratory Distress Syndrome who are on a ventilator. Dexamethasone, on the other hand, is the first medicine to be found to be effective in preserving the lives of COVID-19 patients. The RECOVERY clinical trial, one of the largest studies on COVID-19 treatments, found that this medication reduced the risk of death in hospitalised patients with severe COVID-19 who are on a ventilator or receive oxygen by 20%. ³ Aside from steroids, the virus's effects on the human body are also a concern.

Endothelial activation and changes in endothelial cells have been reported in severe COVID-19 infection who had a massive elevation of von Willebrand factor, which is thought to be caused by endothelial changes have reported multiorgan vascular injury in endothelial cells

and endotheliitis of COVID-19 patients in post mortem studies found severe endothelial cell damage, widespread thrombosis, and microangiopathy in the lungs of COVID. Another element leading to endothelial cell damage and subsequent thrombosis is the inflammatory effects of cytokines generated by SARS-CoV-2 in COVID-19.

The goal of AVN treatment is to relieve discomfort, slow disease development, prevent collapse and restore joint function. There are a variety of therapeutic options for AVN, ranging from conservative to medicinal to surgical, but no defined approach exists. Various medicinal interventions, such as iloprost, nifedipine, and hyperbaric oxygen therapy, have failed to provide significant advantages in the past. As a result, arthroplasty remains the therapy of choice. Although it produces positive results, when done at a young age, it will require at least one correction in the future. Agarwala *et al.* were the first to report the successful use of bisphosphonates for the treatment of AVN in adults. The researchers discovered that bisphosphonates not only improve clinical outcomes but also slow disease progression and reduce the need for surgery. Following that, other authors published papers on the role of bisphosphonates in the management of AVN, and it is currently regarded one of the conventional therapy options for AVN.



Fig 1: AVN1



Fig 2: AVN 2



Fig 3: AVN3

References

1. WHO coronavirus disease COVID-19 Dashboard. Google Scholar.
2. Leung TYM, Chan AYL, Chan EW, *et al.* Short-and potential long-term adverse health outcomes of COVID-19: A rapid review. *Emerg. Microbes Infect.* 2020;9:2190-9. Doi: 10.1080/22221751.2020.1825914pmid:<http://www.ncbi.nlm.nih.gov/pubmed/32940572P> ubMedGoogle Scholar
3. Mahase E. Covid-19: What do we know about long Covid? *BMJ.* 2020;370:m2815. Doi: 10.1136/bmj.m2815pmid:<http://www.ncbi.nlm.nih.gov/pubmed/32665317FREE> Full Text Google Scholar.
4. Ferrari F, Martins VM, Fuchs FD. Renin-Angiotensin-Aldosterone system inhibitors in COVID-19: a review. *Clinics.* 2021;9:e2342:76. Doi: 10.6061/clinics/2021/e2342Google Scholar.
5. IP A, Ahn J, Zhou Y, *et al.* Hydroxychloroquine in the treatment of outpatients with mildly symptomatic COVID-19: A multi-center observational study. *BMC Infect Dis.* 2021;21:72. Doi: 10.1186/s12879-021-05773-wpmid:<http://www.ncbi.nlm.nih.gov/pubmed/33446136PubMedGoogle Scholar>
6. Powell C, Chang C, Naguwa SM, *et al.* Steroid induced osteonecrosis: an analysis of steroid dosing risk. *Autoimmun Rev.* 2010;9:721-43. Doi: 10.1016/j.autrev.2010.06.007pmid:<http://www.ncbi.nlm.nih.gov/pubmed/20621176Cross RefPubMedGoogle Scholar>

7. Agarwala S, Shah S, Joshi VR. The use of alendronate in the treatment of avascular necrosis of the femoral head: follow-up to eight years. *J Bone Joint Surg. Br.* 2009;91:1013-8. Doi:10.1302/0301-620X.91B8.21518pmid:<http://www.ncbi.nlm.nih.gov/pubmed/19651826>CrossRefPubMedGoogle Scholar
8. Agarwala S, Banavali SD, Vijayvargiya M. Bisphosphonate combination therapy in the management of Post chemotherapy avascular necrosis of the femoral head in adolescents and young adults: a retrospective study from India. *J Glob Oncol.* 2018;4:1-11. Doi: 10.1200/JGO.17.00083pmid:<http://www.ncbi.nlm.nih.gov/pubmed/30241233>CrossRefPubMedGoogle Scholar
9. Chan KL, Mok CC. Glucocorticoid-Induced avascular bone necrosis: diagnosis and management. *Open Orthop J.* 2012;6:449-57. Doi: 10.2174/1874325001206010449pmid:<http://www.ncbi.nlm.nih.gov/pubmed/23115605>PubMedGoogle Scholar
10. Jones JP. Osteonecrosis. In: Koopman WJ, ed. *Arthritis and allied conditions: a textbook of rheumatology.* 14th edn. Philadelphia, Pa: Lippincott Williams & Wilkins, 2001: 2143-64. Google Scholar
11. Anderton JM, Helm R. Multiple joint osteonecrosis following short-term steroid therapy. Case report. *J Bone Joint Surg. Am.* 1982;64:139-41. Doi: 10.2106/00004623-198264010-00020pmid:<http://www.ncbi.nlm.nih.gov/pubmed/7054196>FREE Full Text Google Scholar
12. McKee MD, Waddell JP, Kudo PA, *et al.* Osteonecrosis of the femoral head in men following short-course corticosteroid therapy: a report of 15 cases. *CMAJ.* 2001;164:205-6.pmid:<http://www.ncbi.nlm.nih.gov/pubmed/11332313>FREE Full Text Google Scholar
13. Mirzai R, Chang C, Greenspan A, *et al.* The pathogenesis of osteonecrosis and the relationships to corticosteroids. *J Asthma.* 1999;36:77-95. Doi: 10.3109/02770909909065152pmid:<http://www.ncbi.nlm.nih.gov/pubmed/10077138>CrossRefPubMedWeb of Science Google Scholar
14. Assouline-Dayyan Y, Chang C, Greenspan A, *et al.* Pathogenesis and natural history of osteonecrosis. *Semin Arthritis Rheum.* 2002;32:94-24. Doi: 10.1053/sarh.2002.33724bpmid:<http://www.ncbi.nlm.nih.gov/pubmed/12430099>CrossRefPubMedWeb of Science Google Scholar.